REMARKS

Claims 1-4 are pending in the instant application. Claims 1-4 have been rejected. Claim 4 has been amended. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims Under 35 U.S.C. §112

The rejection of claims 1-4 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not disclosed in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention has been maintained. The Examiner suggests that there is no support in the specification for a method for identifying compounds using a reporter with a TGF-beta-dependent promoter within cells expressing specifically interacting proteins with the detection of transcription and the comparison between levels of transcription at precise time points. It is requested that Applicant pointedly express were support can be found in the specification. Moreover, the Examiner maintains that Applicant has not provided sufficient written description for functional mammalian homologues of dCtBP. Applicant respectfully traverses this rejection.

Applicant respectfully disagrees with the Examiner's interpretation of the teachings of the instant specification and of Applicant's reliance on the teachings of Su et al. (submitted with Applicant's response dated April 25, 2005). The basis for meeting the written description requirement is to convey to one of skill in the art that Applicant had possession of that which

is claimed at the time the invention was made. MPEP 2163. Su et al. was provided to the Examiner as evidence of the knowledge of one of skill in the art of screening assays as they pertained to Smad and the TGF-β signaling pathway at the time of filing of the present application. Su et al. teach the use of a luciferase reporter construct containing a TGF-β-dependent promoter with a Smad-binding element (SBE) which is responsive to TGF-β treatment (see page 3139, the paragraph bridging columns 1 and 2) for use in monitoring activity of a test compound (see, *e.g.*, Figure 6). In this regard, page 15 (lines 2-5) of the instant application states that the cell-based reporter assay of the present invention employs "sensitive luminescent substrates for luciferase or β-galactosidase to detect changes in TGF-β-dependent reporter expression in response to specific compounds." This passage clearly conveys to the skilled artisan (*e.g.*, Su et al.) the use of established reagents (*i.e.*, a luciferase reporter and a TGF-β-dependent promoter) and steps (*i.e.*, detect changes in response to specific compounds) required to monitor activity of a test compound in a cell-based assay.

Through the analysis disclosed in the specification, Applicant appreciated that Smad proteins, DNA-binding Smad co-repressor proteins and CtBP proteins interact to mediate repression of genes that are negatively regulated by TGF-β signaling pathways. See page 7, lines 24-28, of the specification. In Figure 6, Applicant exemplifies this interaction using the basic elements of the claimed assay. The assay depicted in Figure 6 employed lacZ (a reporter) under control of the Dpp-dependent (*i.e.*, TGF-β-dependent) *wingless* promoter in cells expressing Mad/Medea (*i.e*, Smad proteins),

Schnurri (*i.e.*, a DNA-binding Smad co-repressor protein), and dCtBP protein.

Having appreciated this mechanism of TGF-β-dependent transcriptional repression, Applicant states at page 7 (lines 8-11) that "The present invention relates to methods for screening or testing of compounds that interfere with TGFβ-dependent transcriptional repression in mammalian cells." In the context of the present invention, TGFβ-dependent transcriptional repression involves the interaction of Smad proteins, DNA-binding Smad co-repressor proteins and CtBP proteins and therefore, as exemplified in Figure 6, these proteins are expressed in the cells being assayed. Accordingly, Applicant has taken the findings presented in the specification and improved upon established cell-based screening assays, such as that of Su et al., to provide the necessary proteins (*i.e.*, Smad proteins, DNA-binding Smad co-repressor proteins and CtBP proteins) to identify compounds that interfere with transcriptional repression of genes induced by a TGF-β, activin or bone morphogenetic protein signal in cells.

By way of corroboration, Applicant submits herewith a Declaration by Dr. Allen S. Laughon which describes the identification of a compound, namely adenovirus E1A protein, that inhibits CtBP thereby interfering with the transcriptional repression of *brk*, which is a direct target of the Medea, Schnurri, dCtBP complex of proteins. This corroborative evidence by Dr. Laughon indicates that the guidance provided by the specification in combination with the well-known assay components successfully yielded the identification of the E1A protein as an inhibitor of CtBP-mediated repression of genes that are

negatively regulated by TGF-β signaling pathways. Thus, in using the assay described in the specification, Applicant has achieved the desired outcome and believes that the specification has conveyed with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicant was in possession of the instant invention.

Regarding the Examiner's rejection of the claims as lacking adequate written description for functional mammalian homologues of dCtBP, Applicant has amended the claims to remove reference to said homologues in an earnest effort to facilitate the allowance of the pending claims.

In light of the present amendments and accompanying remarks, is respectfully requested that the rejections under 35 U.S.C. 112, first paragraph, be reconsidered and withdrawn.

II. Conclusion

The Applicant believes that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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Date: **December 12, 2005**

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